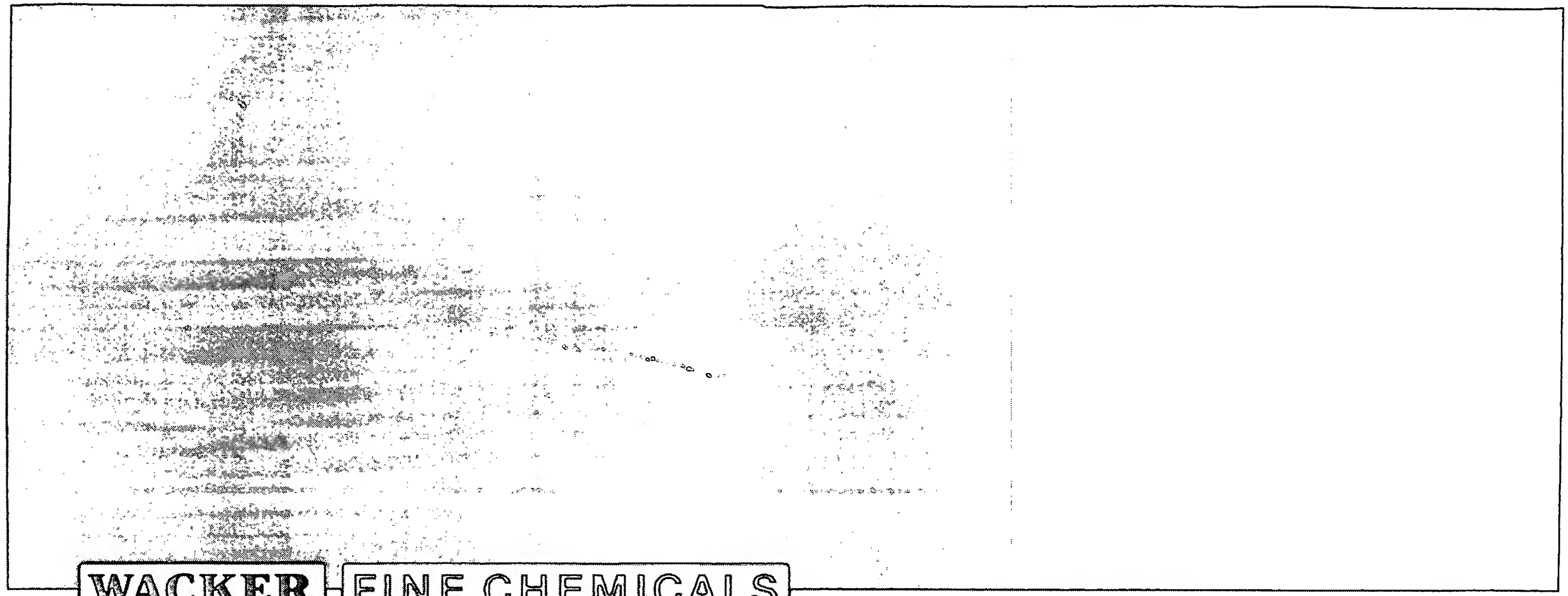


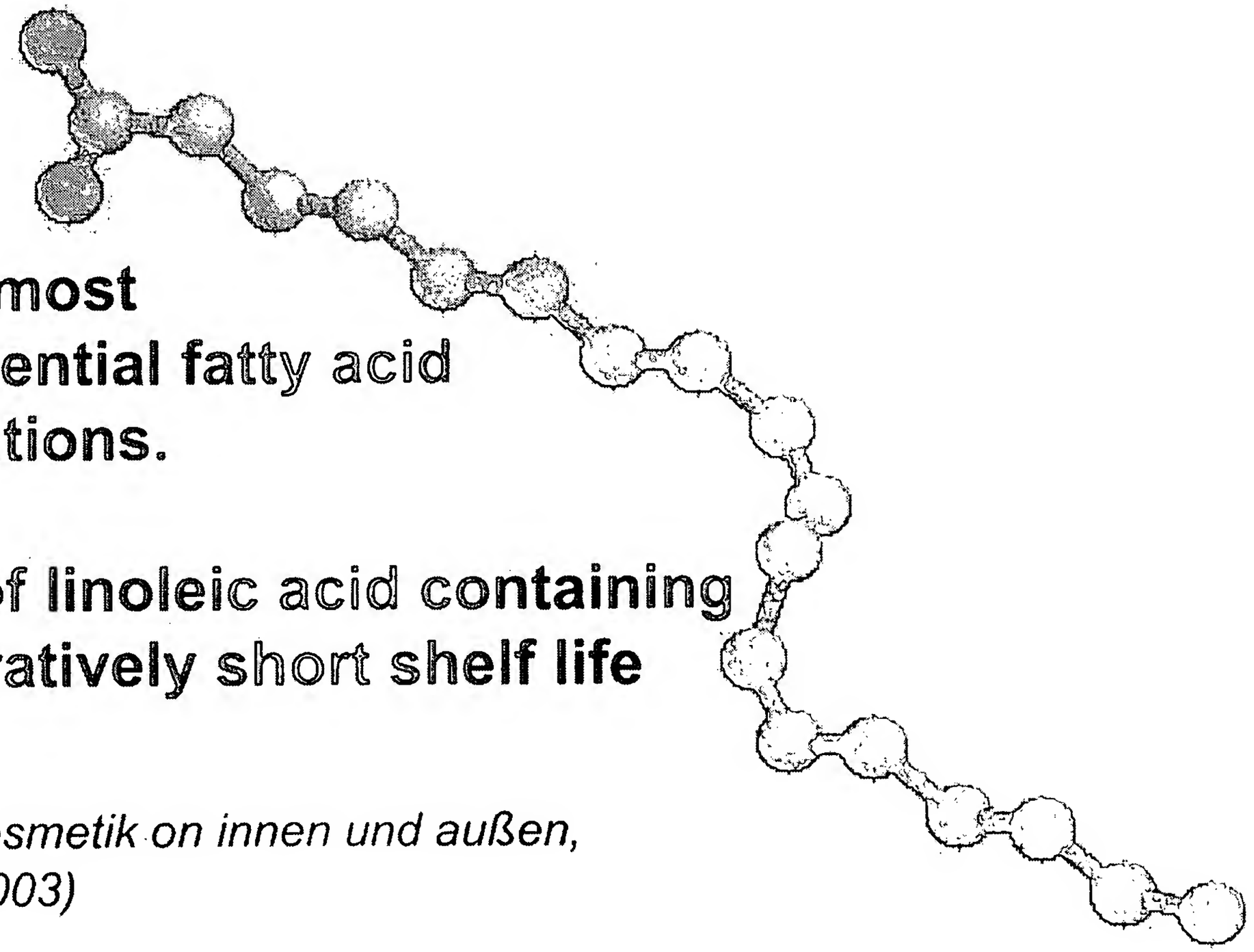
WACKER FINE CHEMICALS

CYCLODEXTRINS ANOTHER TOOL FOR ENCAPSULATION OF LINOLEIC ACID

Regiert Marlies, Kupka Michaela, Sigl Harald, F-I-P, March 2005

CREATING TOMORROW'S SOLUTIONS

LINOLEIC ACID, $C_{17}H_{31}COOH$, E.G. (Z,Z)-9,12-OCTADECADIENOIC ACID

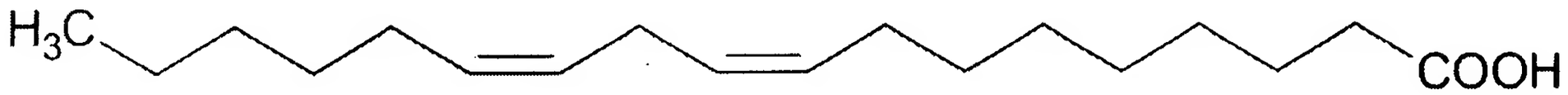


Linoleic acid is the most frequently used essential fatty acid in cosmetic formulations.

One disadvantage of linoleic acid containing oils is there comparatively short shelf life

(Essenzielle Fettsäuren - Kosmetik on innen und außen, Dr. Hans Lautenschläger, 2003)

FUNCTION, PHYSIOLOGICAL EFFECTS



- Belongs to the group of omega-6 fatty acids
- It cannot be synthesized by animals
- Linoleic acid is incorporated in the skin to the most important barrier-active "ceramide I"
  (Essenzielle Fettsäuren - Kosmetik von innen und außen, Dr. Hans Lautenschläger, 2003)
- Is essential for the human body

FUNCTION, PHYSIOLOGICAL EFFECTS

- Is important for the synthesis of eicosanoids,
  which have a regulatory action in various tissues

  (Technical Information BASF,
  „products for the food and pharmaceutical industry", 2002)

- A lack of linoleic acid in the skin has e.g. the effect of:
  - barrier disruption of the skin
  - a higher rate of the trans-epidermal water-loss
  - the skin becomes dry, scale and gets a unhealthy colour

- Acts both as a concentrated energy carrier and
  as a starting material for the synthesis of arachidonic acid
  (important component of cell membranes)

  (Technical Information BASF,
  „products for the food and pharmaceutical industry", 2002)

FUNCTION, PHYSIOLOGICAL EFFECTS

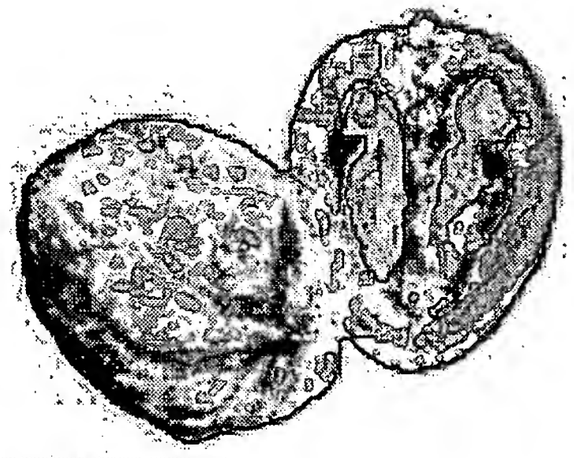
- Requirements / intake recommendations:
  the adult requirement of linoleic acid is 8 – 10g per day
- There is an increased requirement for essential fatty acids after severe accidents and in certain diseases

PROPERTIES AND OCCURRENCE

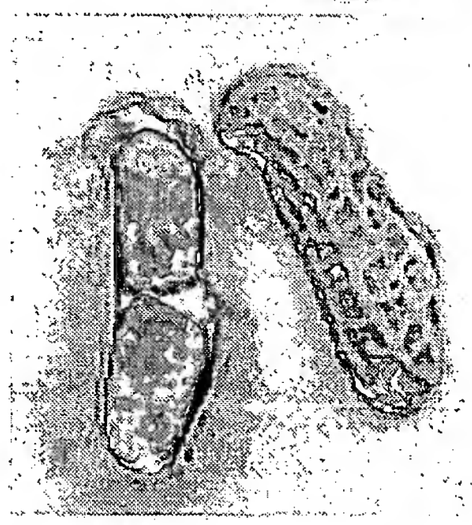
- Is a colorless to straw colored liquid
- Insoluble in water, soluble in oil and fats
- Is the most common polyunsaturated fatty acid
- Linoleic acid also may convert to a isomeric unsaturated conjugated fatty-acid
- It is easily oxidized by air to peroxides that have undesirable biological effects
- Vegetable oils become rancid when exposed to air at room-temperature and can seriously spoil the taste, odor and stability of food products
- It is found in nature in plants and animal tissues

OCCURRENCE

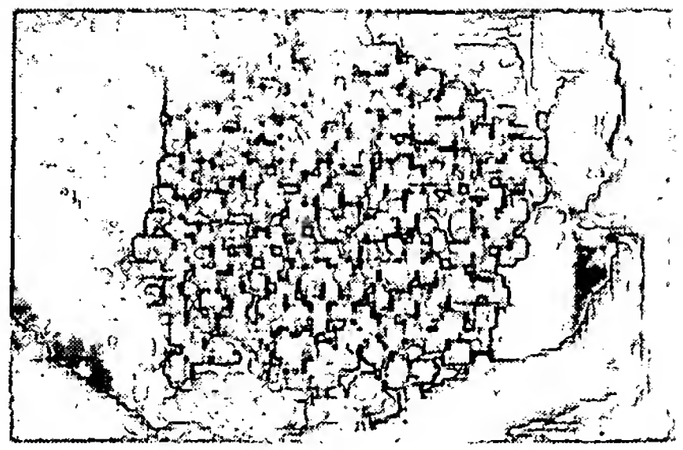
walnut



peanut

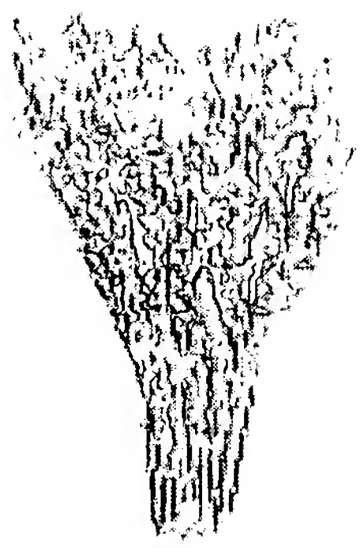


soya

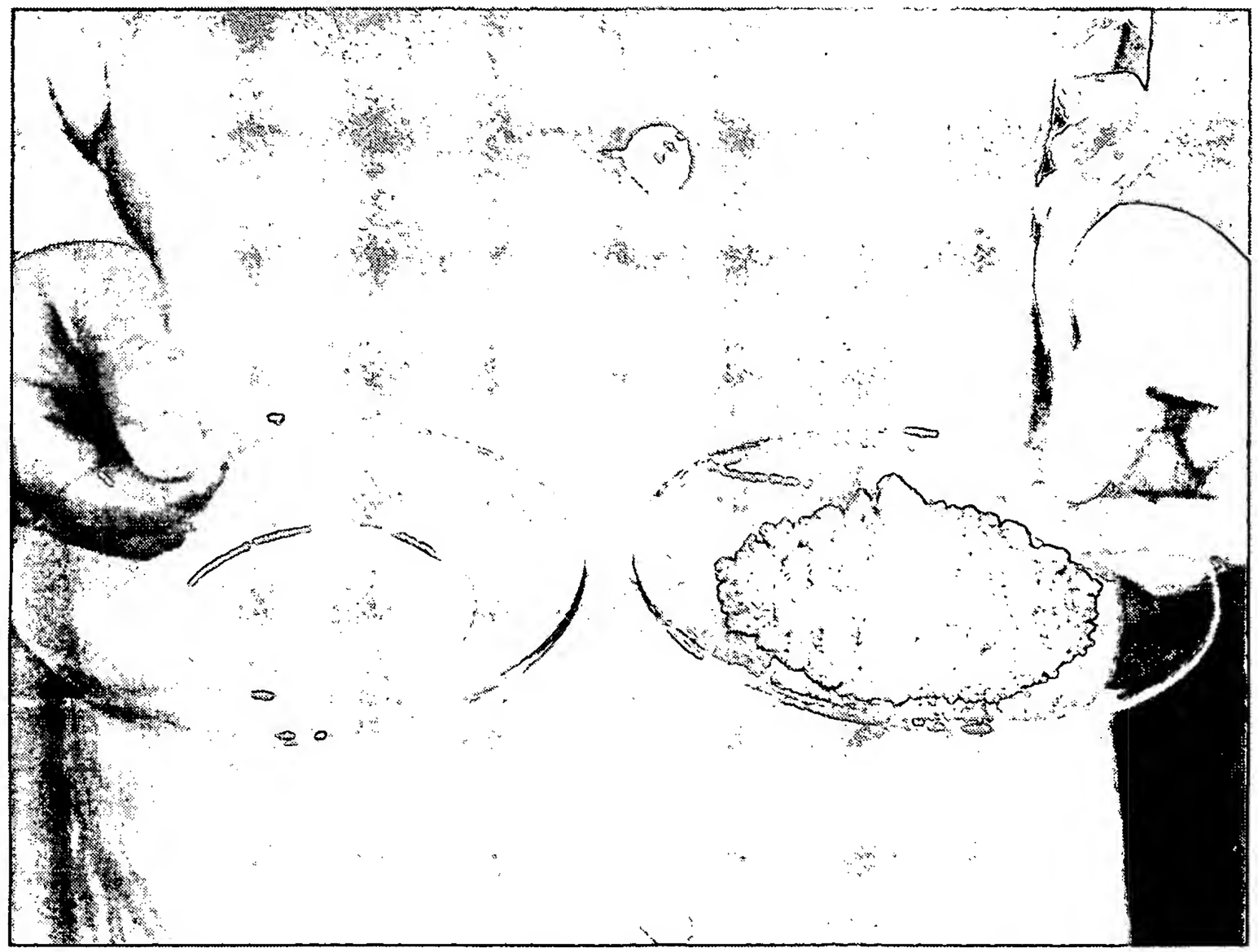


seeds of sunflower

corn



CONVERSION FROM LIQUID TO SOLID COMPLEX



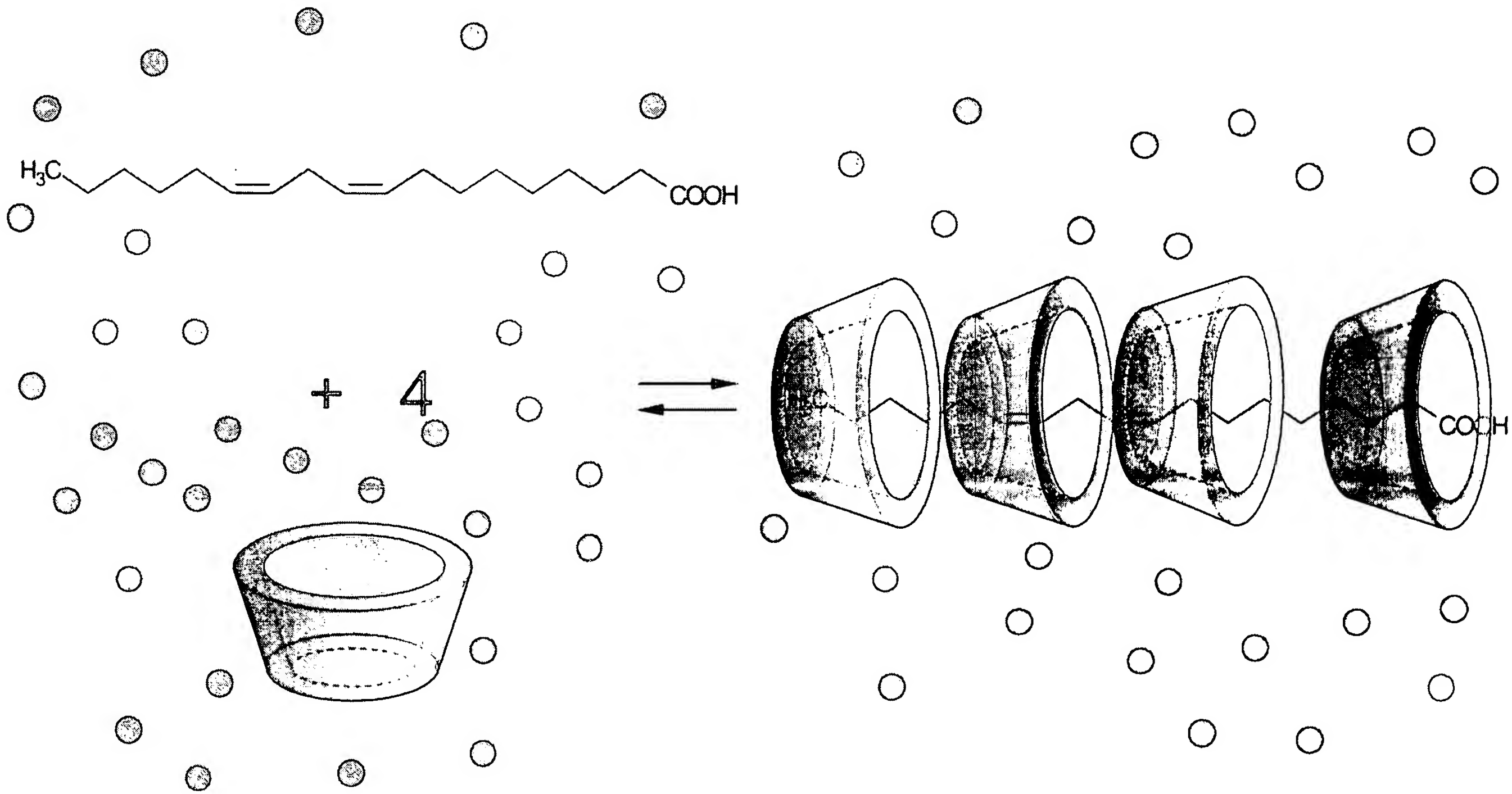
Left:
pure linoleic acid

Right:
CAVAMAX®W6/LINOLEIC ACID-COMPLEX

APPLICATION

- As component in cosmetic formulations like
  - emulsion, cream
  - gel
  - lip-balm
- Colour cosmetic, like lip-stick
  - face powder
  - eye shadow
  - face mask
- As component in derma products
  linoleic acid helps to cure
  - skin disease
  - sun burn
  - burns
  - akne vulgaris

SCHEMATIC REPRESENTATION OF AN INCLUSION COMPLEX FORMATION BETWEEN CYCLODEXTRIN AND LINOLEIC ACID



WACKER FINE CHEMICALS

CYCLODEXTRINS ANOTHER TOOL FOR ENCAPSULATION OF LINOLEIC ACID
Regiert Marlies, F-I-P, February 2007, Slide 9

CAVAMAX® W6/LINOLEIC ACID-COMPLEX, CHARACTERISTICS

	CAVAMAX®W6-Complex
appearance:	white granulate/powder
active content:	min. 7.5 % (NMR, GC)
water content:	max. 14%
INCI names	cyclodextrin/linoleic acid
patent pending	DE10253042.4-4; EP03026137.4; JP 2003-385675; KR 2003-0077579

BENEFITS OF CAVAMAX® W6/ LINOLEIC ACID -COMPLEXES BY APPLICATION IN FORMULATIONS

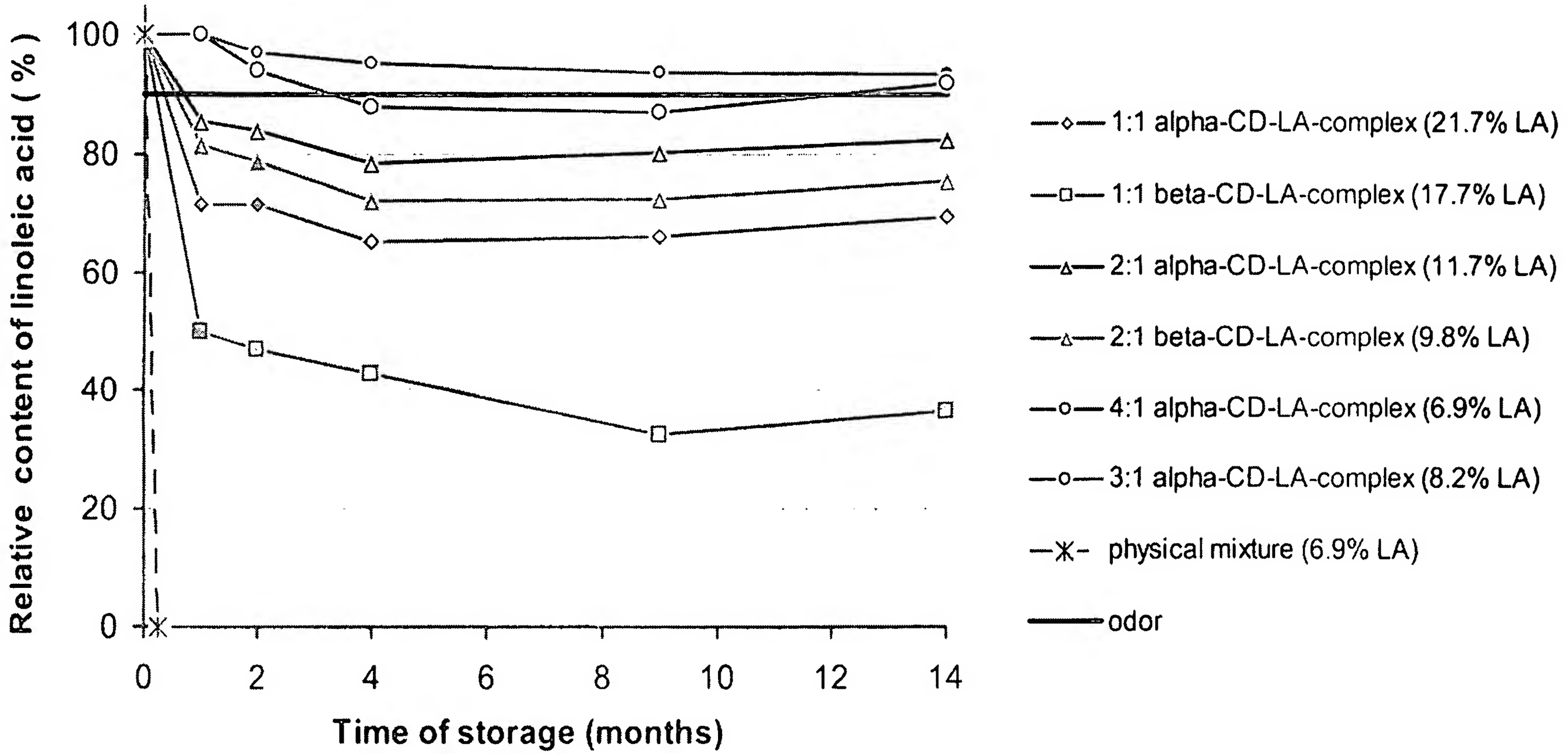
- Improved stability of linoleic acid e.g. oxygen, UV-A and UV-B and temperature
- Controlled release
- No rancidness in finished products e.g. during application
- No need of a stabiliser in cosmetic formulations
- Preparation of cosmetic formulations is even possible at higher temperatures
- Easy handling

BENEFITS OF CAVAMAX® W6/ LINOLEIC ACID-COMPLEXES BY APPLICATION IN FORMULATIONS

- Stable dispersion/emulsion
- Increase of texture of emulsions
- Efficient depot system
- Positive costs/benefit-factor
- Recommended dosage:
  0.5 - 15% of CAVAMAX®W6/LINOLEIC ACID-COMPLEX
- In food products: improved taste and odor stability

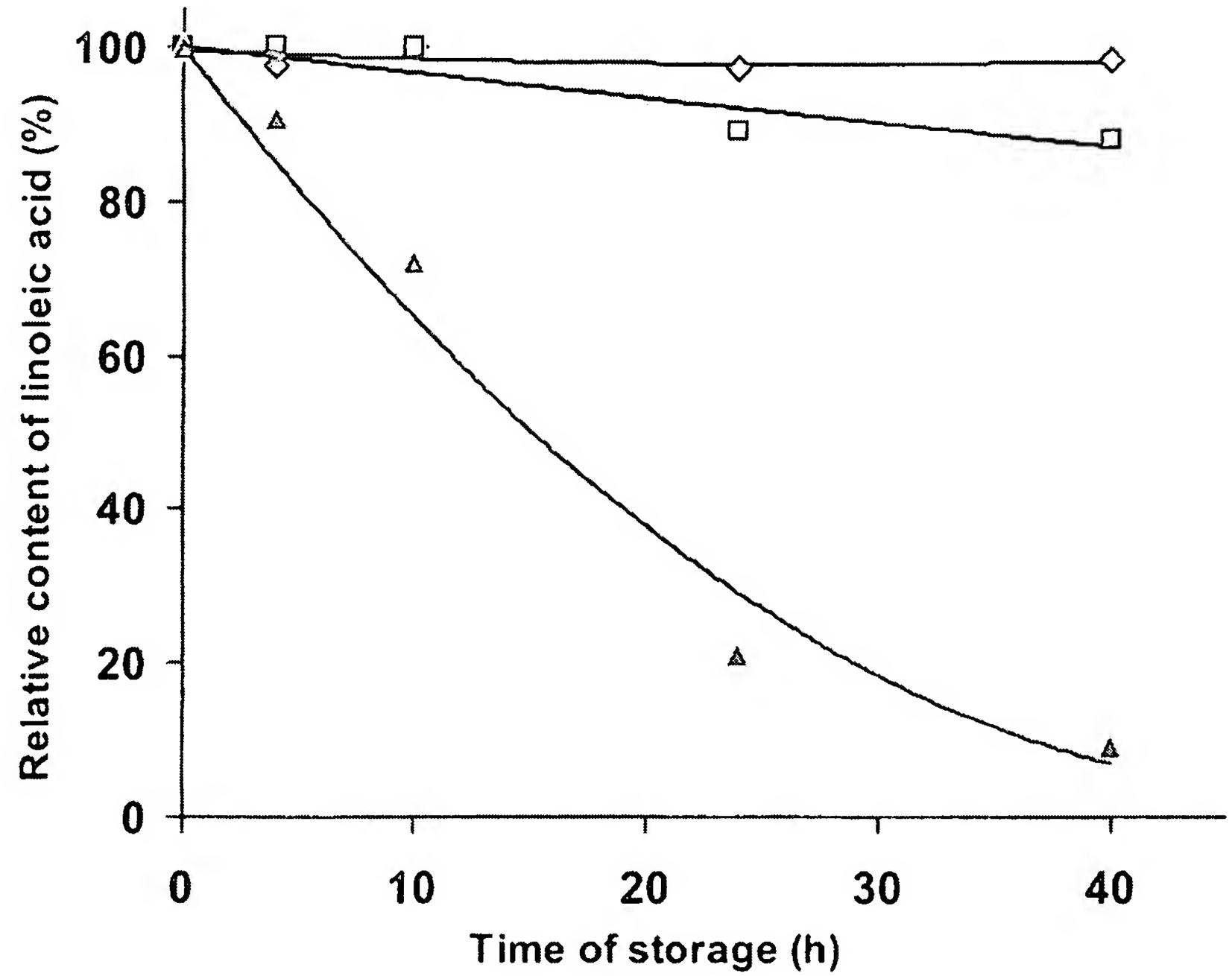
THERMOSTABILITY OF CAVAMAX®/LINOLEIC ACID-COMPLEXES WITH VARIOUS MOLAR RATIO OF ACTIVE AT 45°C

Stability at 45°C, stored in open vessels (90 mm diameter, 3 mm layer)



UV-STABILITY OF COMPLEXED AND UNCOMPLEXED LINOLEIC ACID IN GEL

Stability in Sun Screen Softgel (1.0 % linoleic acid. "suntest" UV-A and UV-B, 45 °C)



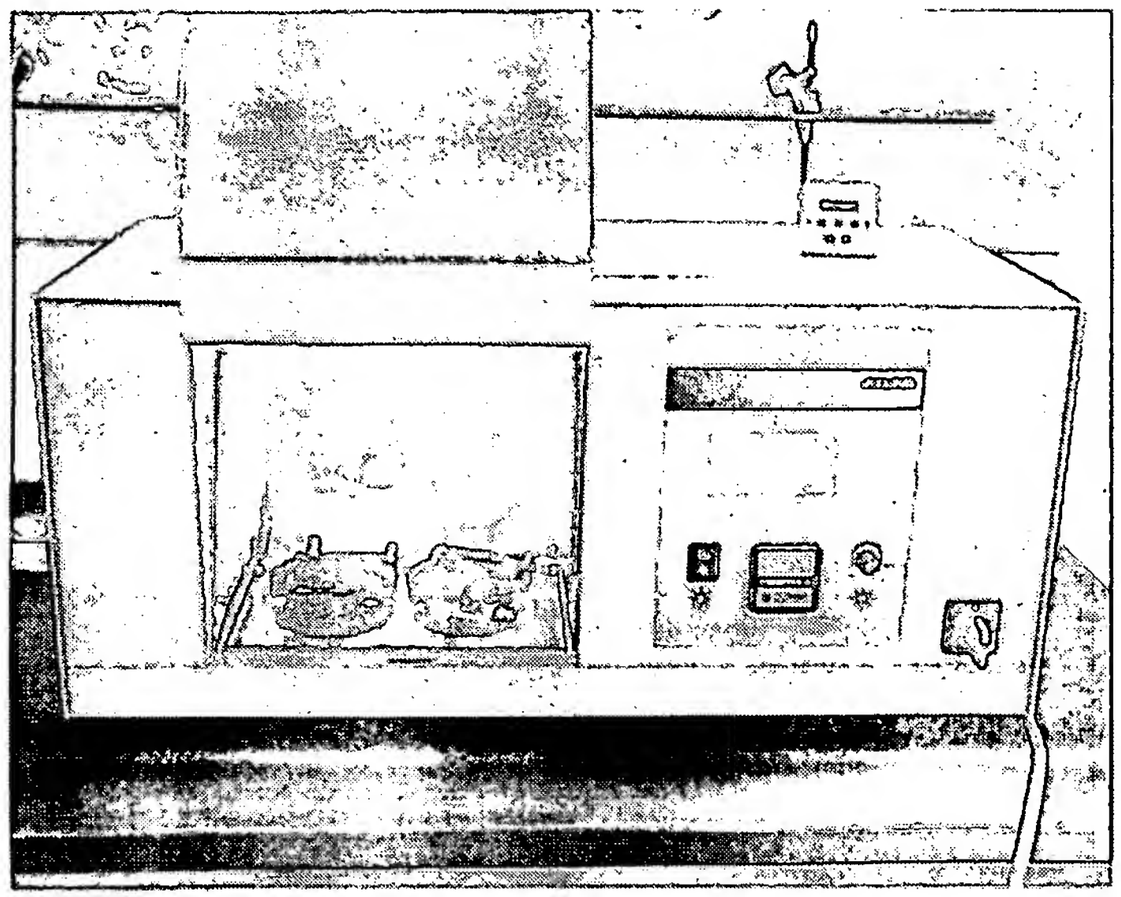
◇ Softgel + 4:1-alpha-cyclodextrin-linoleic acid-complex

□ Softel + 3:1-alpha-cyclodextrin-linoleic acid-complex

△ Softgel + linoleic acid uncomplexed

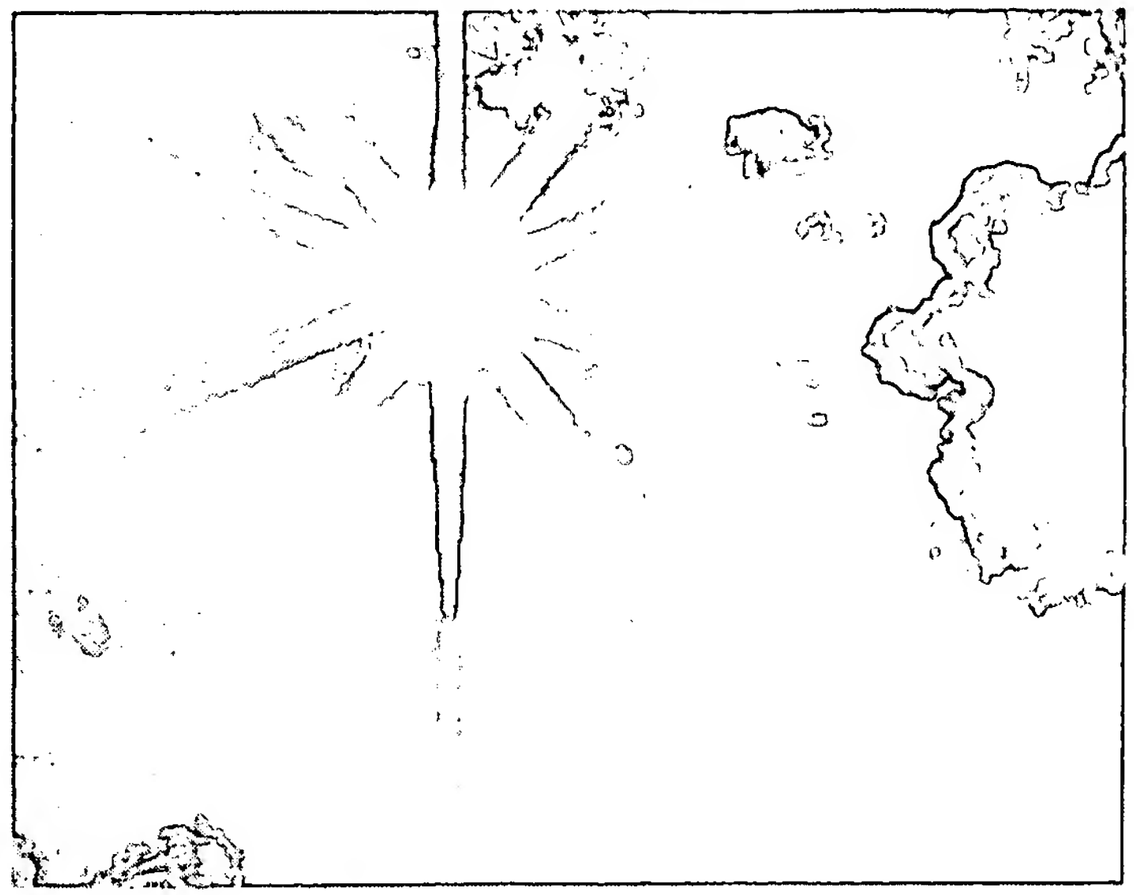
UV-STABILITY TEST IN SUN-TEST DEVICE: COMPARISON

SUN-Test device



max. irradiation/day = 66 MJ/m²

"Sun-Bathing"



irradiation/day (middle europe) = 5.7 MJ/m²

ratio (time lapse factor) =

11 : **1**

UV-A AND UV-B STABILITY TEST IN SUN-TEST EQUIPMENT

Method

Equipment	SUNTEST CPS from ATLAS
Radiation-source	Xenon-Lampe
Optical filter	Solar Standard (filter referring to **COLIPA*** and DIN 67501)
Air cooled sample room	max. determined inside-temperature = 45°C
Maximum radiance	E (300nm – 800nm) = 765W/m²
Constant controlling of the Irradiation	via photodiode

(source: ATLAS-Material Testing Solutions)

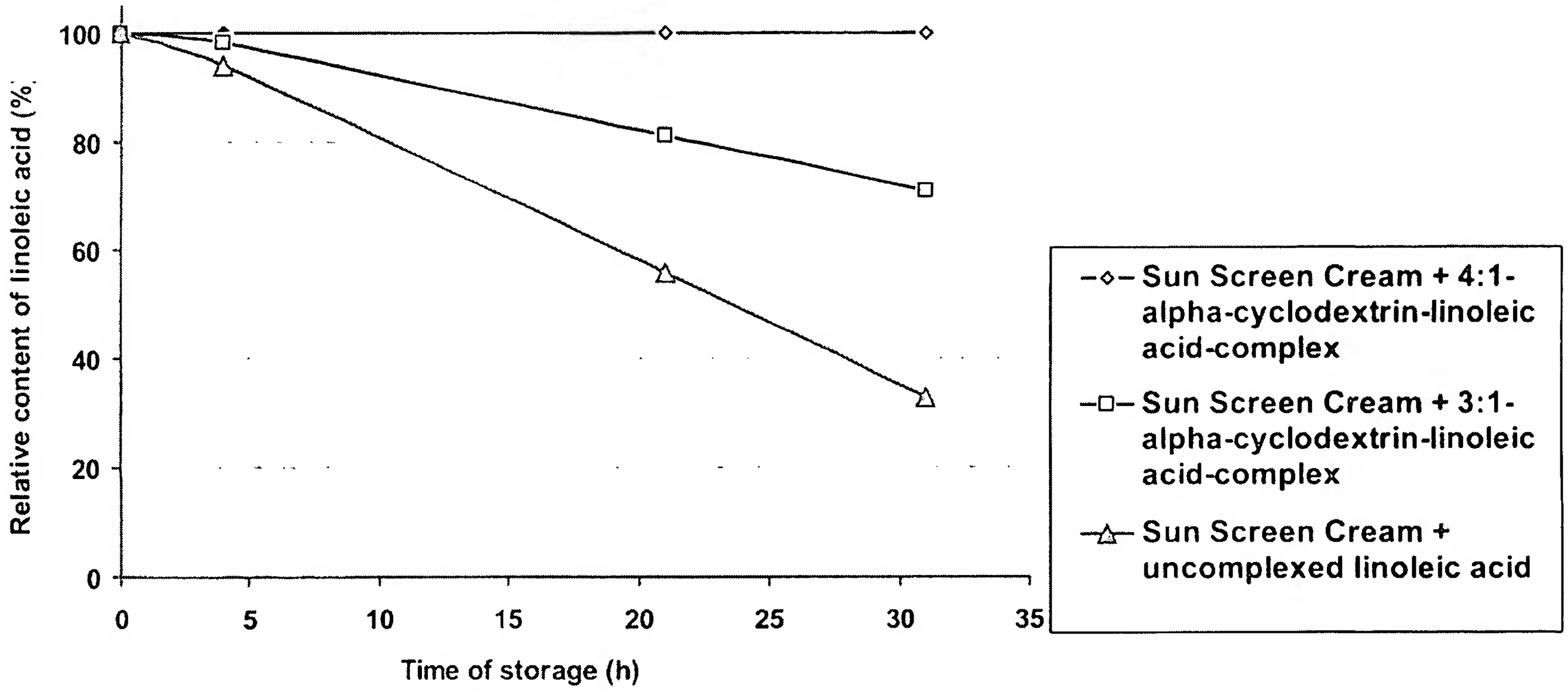
Sample preparation

Solid substance like cyclodextrin-complex
3 – 4 g substance between 2 layers of glass 10 x 10 cm
(glass rim has to be covered with an adhesive tape)

Soft substance like creams und pastes
3 – 4 g in a PE-plastic bag 10 x 10 cm (melted rim)

UV-STABILITY OF COMPLEXED AND UNCOMPLEXED LINOLEIC ACID IN CREAM

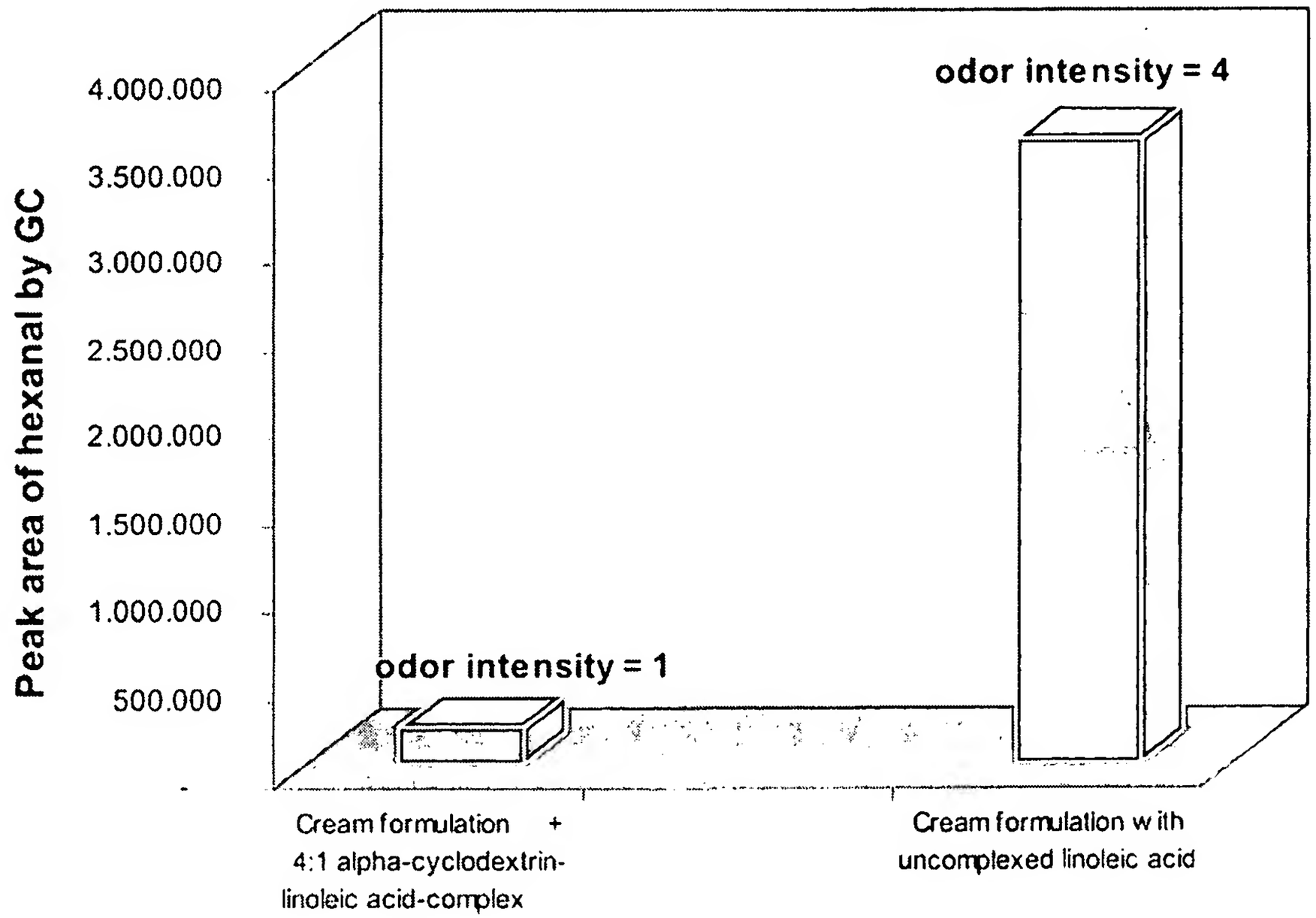
Stability in Sun Screen Cream
(1.0 % linoleic acid content, "suntest" UV-A and UV-B, 45 °C)



LONG-TERM STABILITY OF 1% LINOLEIC ACID AS 4:1-ALPHA-CD/LA-COMPLEX AND UNCOMPLEXED IN CREAM

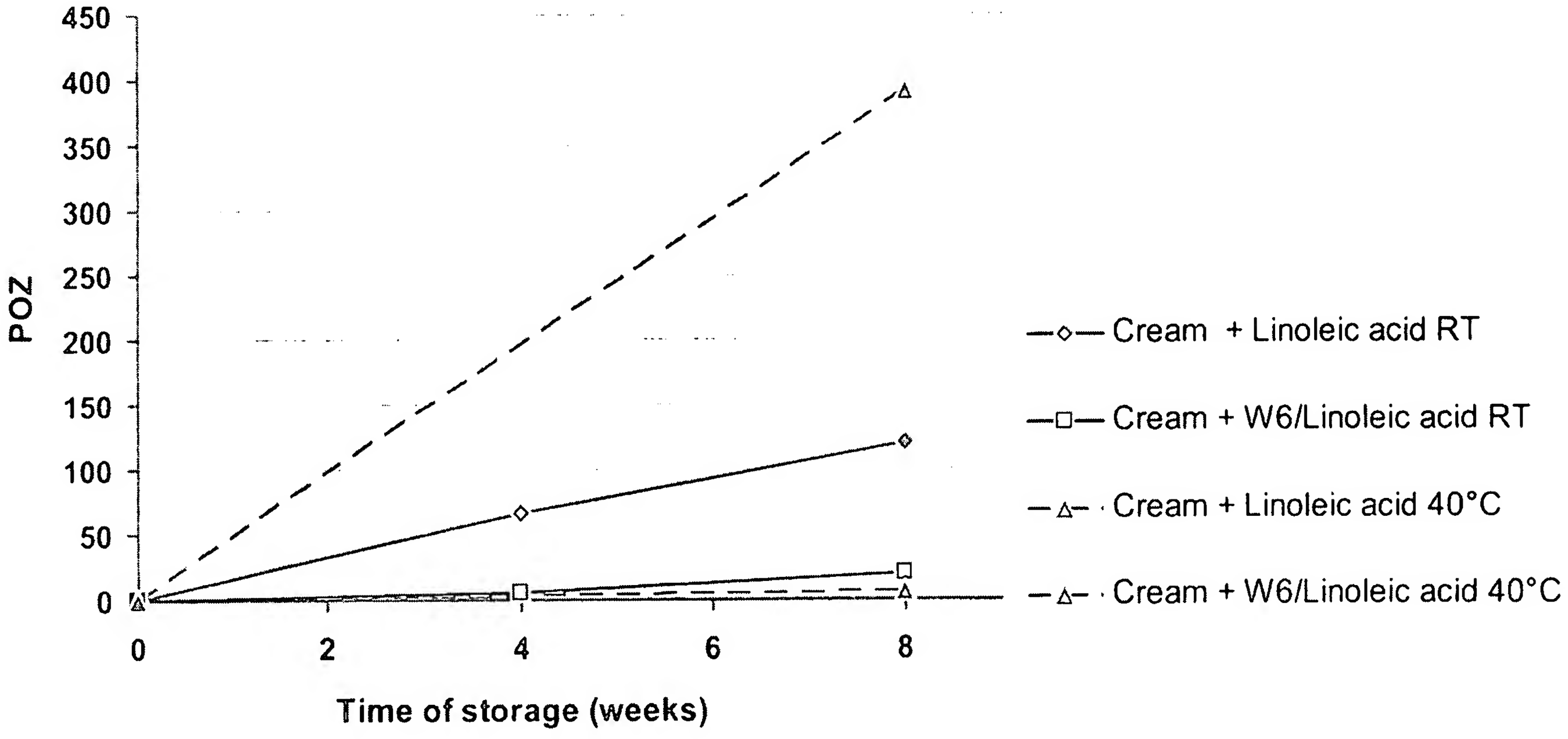
at room temperature after 12 months storage.

Sensory- and SPME/GC-Analysis of deteriorated linoleic acid e.g. as Hexanal



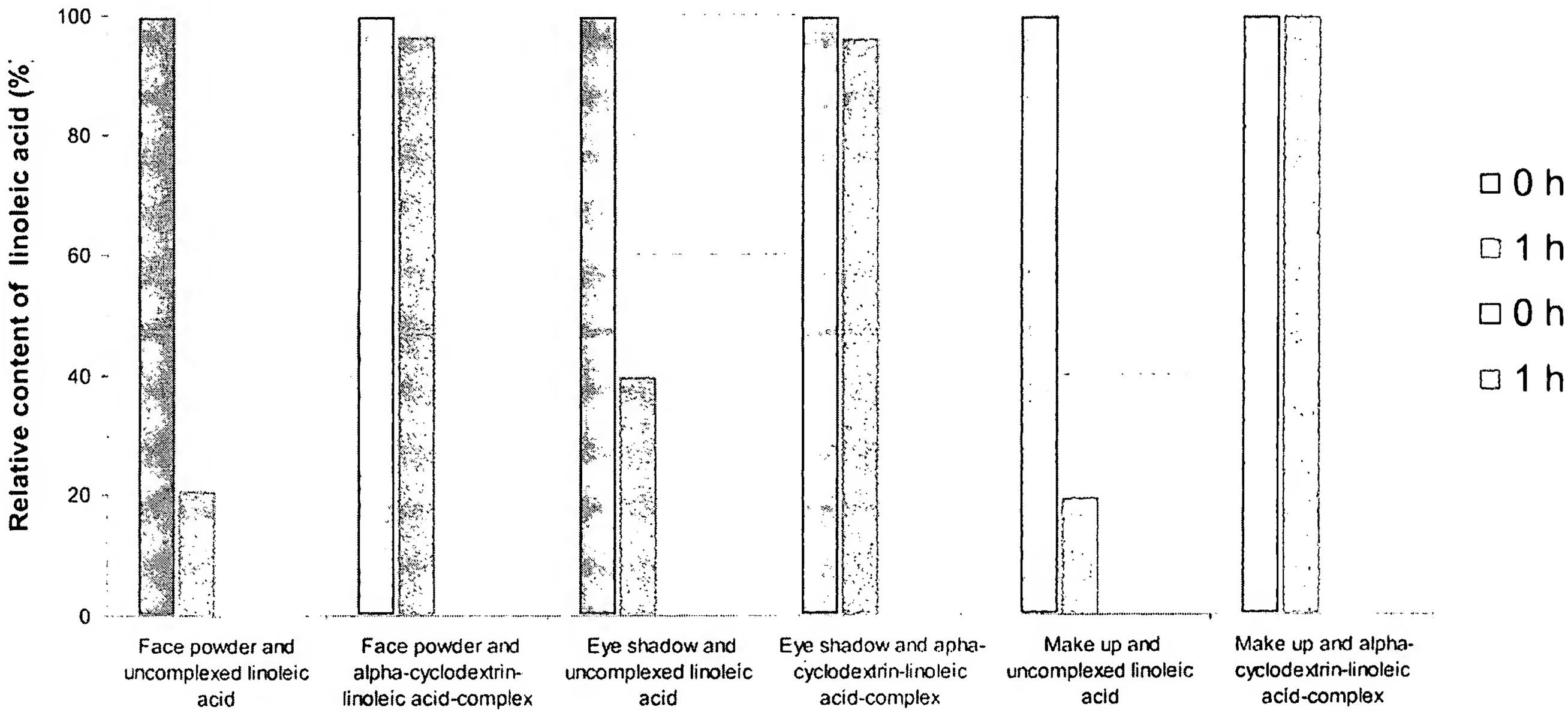
DEGRADATION OF COMPLEXED AND UNCOMPLEXED LINOLEIC ACID BY PEROXIDE VALUE

Instability in Cream W/O stored at different temperatures,
(1.0% linoleic acid content) determined by peroxide value



LIGHT-STABILITY OF 1% LINOLEIC ACID AS 4:1-ALPHA-CD/LA-COMPLEX AND UNCOMPLEXED IN COLOR-COSMETICS

"Sun-Test" UV-A and UV-B at 45 °C; GC-Analysis of Linoleic Acid-Content



DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

Analytical Method

Principle of the Method:	Silylation by MSHFBA, GC-Direct Injection, Internal Standard
Name of the analyte :	Linoleic Acid
Retention times (min) :	Analyte (Linoleic Acid) 8,71 Int.Std. (Eicosanoic Acid) 10,21
Sample name, matrix:	Cyclodextrin or Cosmetic Products
Solvent:	Solvent-Mix 80 % v/v Pyridine + 20 % v/v THF
Quantitation - method :	Internal Standard ISTD
INTERNAL Standard:	Eicosanoic Acid (C20) CAS - NR.: [530-30-9]

Internal Standard solution

Prepare a concentrated (e.g. about 1100 ppm) stock solution of Eicosanoic Acid in the solvent mix. Add a small volume (about 0.8 g) of that stock solution to (about 5g) of the Silylating Reagent MSHFBA to get a ISTD-working solution:
150 ppm ISTD in (MSHFBA > 95 %, < 5% solvent mix).

DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

Sample preparation:

Dissolve the sample (Cyclodextrin 0.1 %, Cosmetic Products 1 %) in the solvent mix (rise in temperature, short ultrasonic agitation).

Silylating Reaction:

200 mg of the sample solution are diluted with 700 mg THF + 100 mg ISTD-working solution = 1000 mg reaction solution with 15 ppm ISTD. Heat the reaction mixture (70 °C, about 15 min) --- Alu Block Heater.

DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

Calibration Range:

Analyte: 5 to 20 mg/kg solvent
ISTD: 15 mg/kg solvent

Calibration solutions:

Prepare solutions of linoleic acid and eicosanoic acid in the pyridine/THF-solvent mix separately and store them in a refrigerator (< 1 month, without silylation).
Dilute and mix the separate solutions to get >= 5 linoleic acid-calibration levels within the calibration range 5-20 ppm with constant 15 ppm ISTD-concentration for all levels.
Silylating Reaction:
Add 10 % (w / w) of the silylating reagent to the calibration solutions. Heat the calibration mixtures (70°C, about 15 min) --- Alu Block Heater.

Reagents:

THF p.A.
Pyridine
MSHFBA, N-Methyl-N-trimethylsilylheptafluorbutyramid (Macherey-Nagel)

DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

GC - Operating Conditions

Instrument:	Gaschromatograph HP 6890 equipped with FID and autosampler			
Column:	30 m x 0. 32 mm ID fused silica capillary column			
Stationary phase:	HP-5 Methyl-Polysiloxan with 5 % Phenyl-Polysiloxan			
Film Thickness:	df = 0,23 µm			
Supplier :	Agilent			
Column temperature:				
Temp. program :	Initial temp.	60 °C	Initial Time	1. 0 min
	Program Rate A	30 °C / min	Program Rate B	- °C / min
	Final Temp.	250 °C	Final Temp.	- °C
	Final Hold Time:	7.0 min	Final Hold Time:	- min
	Analysis Time:	min		
Carrier gas:	Helium			
Column Head Pressure:	117 kPa			
Flow Rate:	1,5 ml / min			
Electronic pressure control:	Constant Pressure			
Injection:	Direct Injection with autosampler HP 7673 A, Splitless mode			

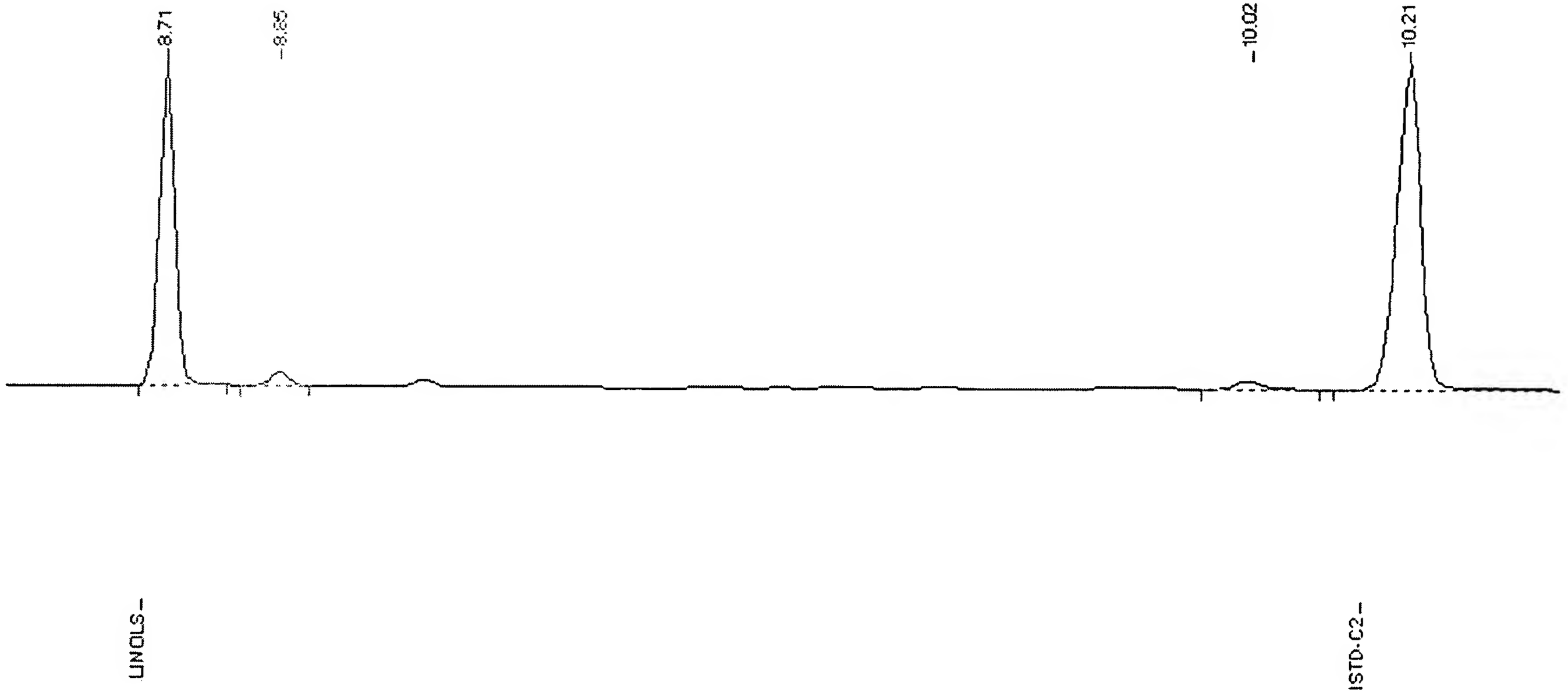
DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

Inject samples:	Silylation reaction mixture of the calibration solutions and of the sample solution, respectively.	
Injektionvolume (µL):	1	
Inlet:	Split/Splitless capillary inlet with EPC	
Temperature:	300 °C	
Split Flow:	100 ml / min	Purge B off 0 min Purge B on 0,9 min
Septum Purge :	3-5 ml / min	
Detector:	FID	Temperature 300°C
Hydrogen:	40 ml/min	
Air :	450 ml/min	
Make up gas:	Helium 29 ml/min	
Data acquisition and quantitation software:	PE Turbochrome	
Appendix:	Representative chromatogram	
Representative GC-Run:	Linoleic acid with Int. Standard Eicosanoic Acid after Silylation	

DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

Representative GC-Run:

Linoleic Acid with Internal Standard Eicosanoic Acid after Silylation



PREPARATION OF A SUN SCREEN SOFT STICK WITH (0.30 W/W%) LINOLEIC ACID

	Ingredients	INCI-Names	w/w	Supplier
A)	Vaseline	Petrolatum	68,9%	
	Wacker Belsil® SDM 6022	Stearoxy Dimethicone, Dimethicone	25,0%	Wacker-Chemie AG
B)	CAVAMAX®W6/LINOLEIC ACID-COMPLEX (7.4% linleic acid)	Cyclodextrin/Linoleic acid	4,0%	Wacker-Chemie AG
	Parsol 1789	Butyl Methoxydibenzoylmethane	2,0%	Givaundan
	Kathon CG	Methylchloroisothiazolinone, Methylisothiazilinone	0,1%	Rohm&Haas
			100,0%	

PREPARATION OF A SUN SCREEN SOFT STICK WITH (0.30 W/W%) LINOLEIC ACID

Calculation:

7.4g linoleic acid are related to 100g complex, 0.296g Linoleic acid related to x g complex

$$\frac{100g \times 0.296g}{7.4g} = 4.0g$$

Preparation:

Heat A to approx. 60°C and mix well, add B at approx. 45°C under stirring for about 15 minutes.

The content of linoleic acid in the formulation is detected by GC.

PREPARATION OF A SUN SCREEN SOFT GEL WITH (0.30 W/W%) LINOLEIC ACID

Ingredients	INCI-Names	w/w	Supplier
A) Water, dd	Aqua	86,8%	
CAVAMAX®W6/LINOLEIC ACID-COMPLEX (7.4% linoleic acid)	Cyclodextrin/linoleic acid	4,0%	Wacker-Chemie AG
Carbopol 940	Carbomer 940	2,5%	Noveon
Wacker Belsil® PDM 20	Phenyl Trimethicone	4,5%	Wacker-Chemie AG
Parsol MCX	Ethylhexyl Methoxycinnamate	2,0%	Givaudan
Kathon CG	Methylchloroisothiazolinone, Methylisothiazilinone	0,20%	Rohm&Haas
		100,0%	

PREPARATION OF A SUN SCREEN SOFT GEL WITH (0.30 W/W%) LINOLEIC ACID

Calculation:

7.4g linoleic acid are related to 100g complex, 0.296g Linoleic acid related to x g complex

$$\frac{100g \times 0.296g}{7.4g} = 4.0g$$

Preparation:

Mix all ingredients at approx. 40°C.

The content of linoleic acid in the formulation is detected by GC.

PREPARATION OF A SUN SCREEN CREAM WITH (0.30 W/W%) LINOLEIC ACID

	Ingredients	INCI-Names	w/w	Supplier
A)	Water, dd	Aqua	60,7%	
	CAVAMAX®W6/LINOLEIC ACID-COMPLEX (7.4% linoleic acid)	Cyclodextrin/linoleic acid	4,0%	Wacker-Chemie AG
	Carbopol 934 Polymer (1% solution)	Carbomer	5,0%	Noveon
	Tetrasodium EDTA	Tetrasodium EDTA	0,20%	
	Glycerine	Glycerine	2,5%	
	Triethanolamine	Triethanolamine	1,0%	
B)	Wacker Belsil® DM 350	Dimethicone	2,0%	Wacker-Chemie AG
	Isopropyl Myristate	Isopropyl Myristate	9,0%	
	Stearyl Alkohol	Stearyl Alkohol	9,5%	
	Cetyl Alkohol	Cetyl Alkohol	0,50%	
	Stearic Acid	Stearic Acid	3,0%	
	Sodium Stearat	Sodium Stearat	1,0%	
	Parsol MCX	Ethylhexyl methoxycinnamate	1,5%	Givaundan
C)	Kathon CG	Methylchloroisothiazolinone, Methylisothiazilinone	0,10%	Rohm&Haas
			100,0%	

PREPARATION OF A SUN SCREEN CREAM WITH (0.30 W/W%) LINOLEIC ACID

Calculation:

7.4g linoleic acid are related to 100g complex, 0.296 g linoleic acid related to x g complex

$$\frac{100\text{g} \times 0.296\ \text{g}}{7.4\ \text{g}} = 4.0\ \text{g}$$

Preparation:

- mix the components of phase A) at 70°C
- mix the components of phase B) at 70°C
- than pour phase A) in phase B) under intense stirring
- after cool down to 45°C add finally phase C)

The content of linoleic acid in the formulation is detected by GC as described

PREPARATION OF A BELSIL FOUNDATION WITH (0.30 W/W%) LINOLEIC ACID

	Ingredients	INCI-Names	w/w	Supplier
A)	Wacker Belsil® DM 1 plus	Dimethicone	10,00%	Wacker-Chemie AG
	Wacker Belsil® CM 7026 VP	C26-28 Alkyl Methicone	2,70%	Wacker-Chemie AG
	Wacker Belsil® SPG 128 VP	Cyclopentasiloxane and Caprylyl Dimethicone Ethoxy Glucoside	11,0%	Wacker-Chemie AG
	Wacker Belsil® DM 5	Cyclomethicone	2,30%	Wacker-Chemie AG
	Hostacerin DGI	Polyglyceryl-2 Sesquiisostearate	2,40%	Clariant
	Wacker Belsil® TMS 803	Trimethylsiloxysilicate	1,50%	Wacker-Chemie AG
B)	Mixture of ferricoxide and titaniumoxide		8,50%	
	Talc	Talc	5,00%	Grolman
C)	Water, dd	Aqua	50,2%	
	Sodium chloride	Sodium Chloride	2,00%	Merck
	CAVAMAX®W6/LINOLEIC ACID-COMPLEX (7.4% linoleic acid)	Cyclodextrin / linoleic acid	4,00%	Wacker-Chemie AG
D)	Fragrance	Perfume	0,30%	
	Kathon CG	Methylchloroisothiazolinone, Methylisothiazilinone	0,10%	Rohm&Haas
			100,0%	

PREPARATION OF A BELSIL FOUNDATION WITH (0.30 W/W%) LINOLEIC ACID

Calculation:

7.4g linoleic acid are related to 100g complex, 0.296 g linoleic acid related to x g complex

$$\frac{100\text{g} \times 0.296\text{ g}}{7.4\text{ g}} = 4.0\text{ g}$$

Preparation:

- mix the components of phase A) at 75°C
- mix the components of phase B) and add to A) under intense stirring
- disperse the complex in phase C) at 50°C
- than pour slowly phase C) to the mixture of phase A) and B)
- after cool down to 45°C add finally phase D)
- than stir till the mixture is homogenous

The content of linoleic acid in the formulation is detected by GC

SUPPLEMENTS

- Page 27, 28, 29, 30, 31, 32 ,33 and 34 on 15.03 2006, adapted formulation recipe
- Page Wacker AG 27, 29, 31 ,33 on 10.08.2006, adapted formulation recipe
- Page 18 revaised
- Page 33 and 34 revaised

CAVAMAX®W6/LINOLEIC ACID - COMPLEX

Consumer expect just high-quality skincare products with extraordinary performance